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Readability and complexity of written information presented to acutely unwell participants for trial consent during the COVID-19 pandemic.

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Abstract:

Introduction: Patient Information Sheet (PIS) and Informed Consent Forms (ICF) are essential tools to communicate and document informed consent for clinical trial participation. These documents need to be easily understandable, especially when used to take informed consent from acutely unwell patients. Health literacy guidance recommends written information should be at a level between

reading age 9 to 11. We aimed to assess the readability and complexity of PIS/ICFs used for clinical trials of acute therapies during the COVID-19 pandemic.

Methods: PIS/ICFs used in trials involving pharmaceutical interventions for COVID-19 during the first year of the pandemic were sourced from hospitals across the UK. PIF/ICFs were assessed for length, approximate reading time and subsection content. Readability and language complexity were assessed using Flesch-Kincaid Grade Level (FKGL) (range 1-18; higher is more complex), Gunning-Fog (GFOG) (range 1-20; higher is more complex) and Flesch Reading Ease Score (FRES) (range 0-100; lower is more complex).

Results: Thirteen documents were analysed with a median length of 5139 words (range 1559–7026), equating to a median reading time of 21.4 minutes (range 6.5–29.3 minutes) at 240 words per minute. Median FKGL was 9.8 (9.1–10.8), GFOG 11.7 (10.4-13) and FRES was 54.6 (47.0–58.3). All documents were classified as 'difficult' for comprehension and had a reading age of 14 years old or higher.

Conclusion: All PIS/ICFs analysed contained literary complexity beyond both recommendations and the reading level of many in the UK population. Researchers should seek to improve communications to improve trial volunteer comprehension and recruitment.

Strengths and limitations of this study

- Analyses PIS/ICF content and readability using commonly used and objective methods.
- Uses transparent and identifiable results at individual trial level
- As a retrospective synthetic analysis, cannot assess actual patient understanding and opinions at the time of illness/recruitment.

What is already known on this topic:

Written information given to volunteers being recruited to clinical trials has been getting longer and more complex.

What this study adds: Patient Information Sheets/Informed Consent Forms used during the COVID-19 pandemic were beyond the reading skills of many volunteers recruited.

How might this study affect research, practice or policy. Researchers, sponsors and ethics committees should take proactive steps to improve written communication in clinical trials, as well as considering supplementary or alternative approaches given the challenges with communication in acute, contagious respiratory illness.

Introduction

The COVID-19 pandemic of 2020 saw research trials set up rapidly to be delivered in acute care settings, often by staff with limited prior trials experience and involving acutely unwell patients. This created new challenges for trials staff and patients. The suitability of the consent processes has been identified as one of the main concerns around the research response to the pandemic(1). Patient Information Sheet (PIS) and Informed Consent Forms (ICF) were adapted from conventional trial templates, following standard UK Medicines and Healthcare Products Regulatory Agency (MHRA) recommendations. Trials staff identified that PIS/ICFs were not suited to the circumstances in which consent and trial discussions actually took place, typically involving staff in masks and personal protective equipment (PPE) and patients who were very unwell, afraid, and isolated from family (1).

Informed consent is both a legal and ethical requirement for healthcare research(2) and is a cornerstone of Good Clinical Practice (3). For trials involving investigational medicinal products (IMPs) there is a legal requirement for written consent to be obtained, unless not physically possible and specifically exempted(4). UK and international guidelines state that the written information provided to participants should support conversations around consent, rather than being the sole source of information(5). This is usually provided in the form of a PIS/ICF, often the only written record provided to patients involved in clinical trials.

Increasing length and language complexity of consent forms may correlate with decreasing participant comprehension (6,7). Despite this, PIS/ICFs have become longer and more complex over time(8), reflecting the requirements of sponsors, ethical review boards and/or recommendations from patients. The implementation of European Union (EU) General Data Protection Regulations (GDPR) has further extended documents(9). Additional considerations regarding consent for samples stored for future use and for genetic testing has added further complexity(10). A consequence of this is that after recruitment clinical trials participants often do not retain an understanding of key components of studies(11,12).

In response to the issues raised by trials staff delivering studies in acute settings during the pandemic, we were interested to review the information provided to trials participants to help understand the problem and identify whether there are better ways to deliver this. The objectives of this study were to describe the written information presented to participants in acute COVID-19 trials in terms of length, content, and readability with a view to improving the process for future studies.

Methods

Patient Information Sheet and Informed Consent Forms for acute inpatient COVID trials across NIHR Respiratory Translational Research Collaboration (TRC) UK sites were screened. Only trials involving investigational medical products were included. PIS/ICFs involving personal legal representative, professional legal representative, or deferred consent, such as for patients lacking capacity, were excluded.

Information sheet and informed consent forms were analysed according to the following parameters:

1. Document length was analysed via total word count. Approximate time-to-read was calculated based on an average reading speed of 240 words per minute (wpm), as well as upper and lower ranges (175-300 wpm). Reading speed estimates are based on analysis by *Brysbaert* for adults reading silently(13).
2. Components of information sheets were reviewed and recorded, and the length of each these assessed by total word count.
3. Language complexity was analysed using the Flesch-Kincaid Grade Level (FKGL) assessment. This metric assesses both word and sentence length and is expressed as a score equivalent to US school grade level reading age (Table 1)(14).
4. Readability was assessed using the Flesch Reading Ease Score (FRES) and the Gunning-Fog Index (GFOG)(15). Both metrics assess readability by analysing word complexity and sentence length. All language complexity and readability analyses were conducted using the software package eadable (Added Bytes Ltd, Horsham, UK, accessed June 2023) (16).
5. Documents were also assessed against the Plain English recommendations for written medical information(17). These consisted of: recommended sentence length 15-20 words; no more than 10% of writing in passive tense; avoiding writing headings in all capitals; avoids underlining; appropriate use of bullet points. Sentence length and passive verb assessment was performed using Microsoft Word (Mac version 16.69.1, performed in June 2023).

Statistical analysis

The analyses are descriptive. Data were tested for normality using the Shapiro-Wilk test, and presented as median (interquartile range).

Patients and the public were not involved in the design of this study.

Age	US Grade Level	English School equivalent	Flesh Kincaid Grade Level	Gunning Fog Index Score	Flesh Reading Ease Score
6-7	1	Year 2	1	1	
7-8	2	Year 3	2	2	
8-9	3	Year 4	3	3	
9-10	4	Year 5	4	4	
10-11	5	Year 6	5	5	90-100
11-12	6	Year 7	6	6	80-90
12-13	7	Year 8	7	7	70-80
13-14	8	Year 9	8	8	60-70
14-15	9	GCSE	9	9	
15-16	10		10	10	50-60
16-17	11	A Levels	11	11	
17-18	12		12	12	30-50
	University (Year 1-3)		13-15	13-15	
	University (Year 4)		16	16	
	Post-graduate		17-18	17-20	0-30
	Post graduate plus			>20	

Table 1: Readability scores with equivalent age, English & US school grades. (15) (18)

Results

We have included information sheets from thirteen clinical trials conducted in 2020-2021 in patients acutely unwell with COVID-19. Three supplied PIS/ICFs were excluded as not meeting inclusion criteria (appendix 1). Of the analysed documents six were phase 2 trials, four were academic phase 3 platform studies, and three were commercial phase 3 studies (appendix 2). Four studies offered trial summary sheets for patients to read prior to the longer PIS/ICF. Translated PIS/ICFs were available for the ReCOVERY trial PIS in 2020, though REMAP-CAP also introduced translated documents for UK use in 2021.

1. Document length

Median (range) word count for the analysed combined PIS and ICF documents was 5139 words (range 1559 – 7026) (Table 2). For a participant with a mean average reading speed (240 wpm) this length equates to a reading time of 21.4 minutes (range 6.5– 29.3 minutes). Participants reading at the lower bound reading speed (175wpm) would take on average 29.4 minutes (range 8.9 – 40.1 minutes). Unlike the other trials included in this analysis, the ReCOVERY trial PIS/ICF contained only generic text on IMP risks and was therefore notably shorter in length.

2. Components of information sheets

Subsection analysis revealed marked variation in length (appendix 3). Information relating to privacy and information governance ranged from 72 to 1159 words in total (reading time 0.3 – 4.0 minutes), with a median of 519 words. The section on risks of participation ranged from 92 to 1189 words (reading time 0.4 - 5.0 mins), with a median of 519. All trials featured a short section on patient benefits of the research (median 48, range 0 -133 words), except for the ACCORD-2 platform study.

3. Language complexity

All information sheets featured notable language complexity, median (range) 9.8 (9.1 – 10.8), with no document scoring lower than a Flesch-Kincaid Grade Level of 9, equivalent to that of a 14-15 year old (Table 1).

4. Readability

None of the included PIS scored above 60 on FRES, with a median (range) score of 54.6 (47.0 – 58.3). Scores below 60 are considered 'difficult'. Assessing readability using the alternative measure the Gunning-Fog index (GFOG), the documents had a median (range) score of 11.7 (10.4 – 13.0).

5. Use of plain English

Three out of thirteen trial PIS had an average sentence length greater than 20. All trial PIS exceeded the recommended 10% writing in passive tense, with a median (range) of 40% (22% - 41%). Three out of 13 trials presented headings in capitals, while two out of 13 trials did not use bullet points. 10 trials used underlining. No trial met all five assessed Plain English recommendations (appendix 4).

Trial	Total pages (PIS+ICF)	Total Words	Reading Time (minutes)			Flesch-Kincaid Grade Level[1]	Gunning-Fog score[2]	Flesch Reading Ease Score[3]	Average Sentence Length (words)
			175 wpm (lower bound)	240 wpm (mean)	300 wpm (upper bound)				
Phase III Academic (Platform trials)									
ReCOVERY	2 + 2	1559	8.9	6.5	5.2	9.9	12.2	55.2	20.5
REMAP-CAP	8 + 2	3688	21.1	15.4	12.3	10.5	12.1	48.2	18
TACTIC-E	13 + 3	5685	32.5	23.7	19.0	10.6	12.4	49.1	20.5
TACTIC-R	9 + 3	4994	28.5	20.8	16.6	10.8	12.7	48.9	20.1
Phase III Commercial									
GS-US-540-5773	13 + 3	5139	29.4	21.4	17.1	9.1	10.6	57.8	19.4
RUXCOVID	14 + 4	6855	39.2	28.6	22.9	9.2	10.4	55.0	18.5
SPRINTER	12 + 2	5467	31.2	22.8	19.1	9.8	11.8	54.4	20.4
Phase II									
ACCORD-2	14 + 4	7026	40.1	29.3	23.4	10.0	11.9	54.6	19.1
COVASE	5 + 2	3544	20.3	14.8	11.8	9.7	11.3	54.8	18.9
ILEAD-7	10 + 2	4626	26.4	19.3	15.4	11.2	13.0	47.0	20.6
OSCAR GSK	20 + 5	6046	34.5	25.2	20.2	9.3	11.6	56.5	16.3
SYNAIRGEN SG016	15 + 3	6455	36.9	26.9	21.7	9.0	11.2	58.3	18.9
Theravance 0188	10 + 2	4468	25.5	18.6	14.9	9.7	11.6	54.2	18
Overall									
Median	12.5 + 3	5139	29.4	21.4	17.1	9.8	11.8	54.6	19.1

Table 2: Summary of document length and complexity for clinical trial patient information sheets (PIS) and investigator consent forms (ICF) for clinical trials conducted during acute COVID-19 infection. [1]Range 0-18, higher score is more complex, recommended ≤6. [2]Range 0-20, higher score is less readable, recommended ≤6. [3]Range 0-100, 100 is best readability, recommended ≥60.

Discussion

In this study we have analysed the information provided to acutely unwell patients undergoing recruitment to trials of new therapies for COVID-19. The pandemic was an unprecedented international health emergency, and there was urgent need for potential therapies to be trialled in these settings. However, trials staff identified that consent processes were often ill suited to the acute settings in which they were delivered, and our results would appear to support these subjective observations. Median length was 5303 words, equivalent to a reading time of 21.4 minutes, though this is likely an underestimate of the true time patients would require. Reading time estimates are derived from studies in healthy volunteers and do not take into account pauses or re-reading of sections(13). There is no data available quantifying the impact of acute illness states on reading speed or accuracy. In this state median reading time may be nearer the lower reading speed estimate of 29.6 minutes.

Long and complex PIS/ICFs are not unique to this clinical scenario with similar findings for paediatric trials(19), surgical trials(20) and trials conducted in emergency departments(21). *O'Sullivan* analysed 176 PIS/ICFs used in the UK and Ireland up to 2019, demonstrating readability metrics similar to those found in this analysis(9). Similar issues were also identified by a US study looking at consent and patient information for COVID vaccine studies, where subjects have the benefit of being able to consider the trial and the information presented about it(22). This highlights that these acute COVID studies had very little adaptation for the acute scenario from standard practice. While the longest and most complex documents were phase II trials, this was not universal with three phase II trials being below the overall median for both length and four for language complexity.

Literacy skills in the United Kingdom vary widely. The UK Government Skills for Life survey in 2011 found that 15% of people in England aged 16-65 had reading ability below adult literacy 'level 1', broadly equivalent to a reading age of 12-14 years old. Accordingly 1 in 6 individuals would not attain a grade D-G at GCSE level English and would likely struggle to read a train timetable or a pay slip(23). In contrast, the information provided in the trial patient information sheets had a median complexity equivalent to age 14-15 years and median readability was equivalent to age 16-17 years.

Written PIS are only one part of the consent process, and informed consent also involves a trained health professional delivering the information and contextualising this for participants. In normal practice this is relatively straightforward, involving discussion with the patient, sometimes with family members too, to ensure that they understand the study, including risks and benefits. In the specific context of the COVID-19 pandemic however staff were required to wear PPE, including masks and face protectors. While necessary to protect staff, studies have shown that wearing PPE, particularly masks,

have a negative effect on speech discrimination and comprehension(24,25). For this reason, providing clear and accessible written information for COVID-19 trials was even more important.

During the early months of the pandemic there were no approved therapies for COVID-19, beyond best supportive care. Patients in the UK did not have access to the wide range of therapies that were being proposed and offered elsewhere without trial evidence. The only way of accessing such treatments was in the context of a trial, and patients may have felt particularly incentivised to take part in trials because of this. This may have mitigated against impact of information being only partially understood. It does not detract however from the need to reflect on this aspect of clinical trials in order to understand how to improve the information provided in acute settings.

Four of the included studies also provided a trial summary sheet for patients, so that they could review the most important points of the trial without reference to the much longer full PIS. No other forms of information were available, and none of the studies made use of video explainers for patients or family members (although some, like the ReCOVERY study, did offer similar information online). Future trials may consider looking at how to use such resources to better inform patients, and clinical trial templates for acute settings might benefit from being more concise and focussed. To support rapid progression of medical knowledge during pandemics or other national emergencies, there might be a case for more streamlined consent processes. For example, a two-stage consent might present the most important points only in the acute presentation, followed by a review of consent and confirmation of participation during convalescence.

This study has only looked at the information provided to patients in written form, and a limitation is that we are unable to assess now how this was viewed and retained by patients at the time. We have also only looked at information provided in English, and the analyses of reading time and complexity all assume that English is the reader's first language. We are unable to assess how many patients would have had added difficulty because this was not the case. No data are available on how many, if any, patients were excluded by inability to fully comprehend written or verbally provided information. Only the two major platform studies had translated documents available. The ReCOVERY trial allowed telephone translations if a patient's native translation was not available in written form, though no others did. We are also aware of sites being unwilling to enrol patients without endorsed written documents. *Murali* showed Asian, Black and Mixed ethnic groups were underrepresented in UK Covid-19 trials(26).While the causes of this are multifaceted, it is likely that language issues were a contributory factor. We have deliberately not compared these consent forms to those used in other acute settings, since the primary focus was to address how consent was delivered during COVID-19 to reflect how we can better manage future pandemics. These finding are however likely generalisable to other acute settings. There are valid criticisms of synthetic readability metrics. Rewritten

documents with improved readability scores do not always improve participant comprehension(27). Nonetheless their use has been endorsed to guide improvements in readability of PIS/ICFs following consensus meetings(28).

In summary, we have shown that clinical trial participant information sheets are lengthy, take significant time to read under optimal conditions, and regularly exceed recommendations on complexity and language. In acute settings it is especially important to make the communication of trials information clear and understandable. Patient information and consent was identified as being an area for improvement by clinical trials staff. In collaboration with patients and public contributors, proportionate information sheets for acute settings need to be developed with alternative consenting models considered which include multi-step process where complex information is only delivered when patients are well enough to consider it.

Author Contributions

Conceptualisation by AH. Data collection and initial analysis by EG. Manuscript initially drafted by EG and AH. Significant critical review and further development of manuscript by all authors. All authors approve final copy. AH is the guarantor of this work.

Competing Interests

MB reports unrestricted research grants from AstraZeneca and Roche, and has received honoraria to her institution for speaker's fees from AstraZeneca, Chiesi, Cipla and GlaxoSmithKline. She is a scientific adviser to Albus Health and ProAxsi. CEB reports fees to his institution from AZ, GSK, Novartis, Chiesi, BI, Genentech, Roche, Sanofi, Regeneron, Mologics, 4DPharma, Synairgen, Merck. JCD reports reports grants from CF Trust, CF Foundation, CF Ireland, EPSRC and personal fees Vertex Pharmaceuticals, Boehringer-Ingelheim, Eloxx, Algipharma, Abbvie, Arcturus, Enterprise Therapeutics. RAE reports grants from NIHR/UKRI/Wolfson Foundation; consulting fees from AstraZeneca; lecture honoraria from Boehringer; travel support from Chiesi. LPH reports grants from MRC. SM reports grants from BLF, MRC, June Hancock Mesothelioma Research, Alpha-1 Foundation, and Myrovlytis Trust. NM reports unrestricted research grants from and sits on paid advisory boards for Rocket Medical Plc and BD. JCP reports grants from UKRI, LifeArc and MRC. ES reports reports grant funding from NIHR, MRC, HDR-UK, Innovate UK, British Lung Foundation and Alpha 1 Foundation. SS reports speaker fees from GSK, AstraZeneca, Chiesi, Boehringer Ingelheim, and Novartis; participates on advisory boards for GSK, AstraZeneca, Chiesi, Boehringer Ingelheim, Novartis, Knopp Biotech, Munipharma, ERT Medical, and Owlstone Medical; is a member of the European Respiratory Society Science Council and the UK Medical Research Council; and is a cofounder of Eupnoos Ltd. TW reports grants from UKRI, Synairgen, AZ, UCB, Bergenbio and personal fees from Synairgen and Valneva. ARH reports grants from JP Moulton Charity, CF Trust, CF Foundation, MRC and UKRI and personal fees from Vertex Pharmaceuticals and Mylan Pharmaceuticals

References

1. Horsley AR, Pearmain L, Knight S, Schindler N, Wang R, Bennett M, et al. Large scale clinical trials: lessons from the COVID-19 pandemic. BMJ Open Respir Res. 2022 Jun;9(1):e001226.

2. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Jama. 2013;310(20):2191–4.

3. ICH guideline for good clinical practice E6(R2) [Internet]. INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE (ICH); 2016 [cited 2023 Apr 2]. Available from: https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf

4. Informed consent in clinical trials [Internet]. UK Health Research Authority; 2008. Available from: www.hra.nhs.uk/media/documents/informed-consent-in-ctimps.pdf

5. General Principles - Consent and Participant information sheet preparation guidance. [Internet]. [cited 2023 Feb 13]. Available from: https://www.hra-decisiontools.org.uk/consent/principles-general.html

6. Grundner TM. On the Readability of Surgical Consent Forms. N Engl J Med. 1980 Apr 17;302(16):900–2.

7. Epstein LC. Obtaining Informed Consent: Form or Substance. Arch Intern Med. 1969 Jun 1;123(6):682.

8. Albala I, Doyle M, Appelbaum PS. The evolution of consent forms for research: a quarter century of changes. IRB Ethics Hum Res. 2010;32(3):7–11.

9. O'Sullivan L, Sukumar P, Crowley R, McAuliffe E, Doran P. Readability and understandability of clinical research patient information leaflets and consent forms in Ireland and the UK: a retrospective quantitative analysis. BMJ Open. 2020 Sep 1;10(9):e037994.

10. Code of Practice and Standards - Code E : Research [Internet]. Human Tissue Authority; 2017 [cited 2023 Nov 21]. Available from: https://content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf

11. Foe G, Larson EL. Reading Level and Comprehension of Research Consent Forms: An Integrative Review. J Empir Res Hum Res Ethics. 2016 Feb;11(1):31–46.

12. Kelly CM, Feighery R, McCaffrey J, Higgins M, Smith M, O'Reilly S, et al. Do oncology patients understand clinical trials? A nationwide study by Cancer Trials Ireland. Ann Oncol. 2017 Sep;28:v643–4.

13. Brysbaert M. How many words do we read per minute? A review and meta-analysis of reading rate. J Mem Lang. 2019 Dec;109:104047.

14. Jindal P, MacDermid J. Assessing reading levels of health information: uses and limitations of flesch formula. Educ Health. 2017;30(1):84.

15. Kincaid JP, Fishburne Jr, Robert P. R, Richard L. C, Brad S. Derivation of New Readability Formulas (Automated Readability Index, Fog Count and Flesch Reading Ease Formula) for Navy Enlisted

Personnel: [Internet]. Fort Belvoir, VA: Defense Technical Information Center; 1975 Feb [cited 2023 Feb 13]. Available from: http://www.dtic.mil/docs/citations/ADA006655

16. Readable [Internet]. [cited 2023 Feb 13]. Test your readability. Available from: https://readable.com/

17. Medical information [Internet]. [cited 2023 Feb 13]. Available from: https://www.plainenglish.co.uk/medical-information.html

18. Flesch R. The Art of Readable Writing (Reissue). Wiley-Hungry Minds; 1949.

19. Nash E, Bickerstaff M, Chetwynd AJ, Hawcutt DB, Oni L. The readability of parent information leaflets in paediatric studies. Pediatr Res. 2023 Sep;94(3):1166–71.

20. Karimi AH, Guyler MR, Hecht CJ, Burkhart RJ, Acuña AJ, Kamath AF. Assessing the Readability of Clinical Trial Consent Forms for Surgical Specialties. J Surg Res. 2024 Apr;296:711–9.

21. Mader TJ, Playe SJ. Emergency Medicine Research Consent Form Readability Assessment. Ann Emerg Med. 1997 Apr;29(4):534–9.

22. Emanuel EJ, Boyle CW. Assessment of Length and Readability of Informed Consent Documents for COVID-19 Vaccine Trials. JAMA Netw Open. 2021 Apr 28;4(4):e2110843.

23. 2011 Skills for Life Survey: A Survey of Literacy, Numeracy and ICT Levels in England. 2011;

24. Round M, Isherwood P. Speech intelligibility in respiratory protective equipment - Implications for verbal communication in critical care. Trends Anaesth Crit Care. 2021 Feb;36:23–9.

25. Hampton T, Crunkhorn R, Lowe N, Bhat J, Hogg E, Afifi W, et al. The negative impact of wearing personal protective equipment on communication during coronavirus disease 2019. J Laryngol Otol. 2020 Jul;134(7):577–81.

26. Murali M, Gumber L, Jethwa H, Ganesh D, Hartmann-Boyce J, Sood H, et al. Ethnic minority representation in UK COVID-19 trials: systematic review and meta-analysis. BMC Med. 2023 Mar 29;21(1):111.

27. Grady C, Touloumi G, Walker AS, Smolskis M, Sharma S, Babiker AG, et al. A randomized trial comparing concise and standard consent forms in the START trial. Woolfall K, editor. PLOS ONE. 2017 Apr 26;12(4):e0172607.

28. Coleman E, O'Sullivan L, Crowley R, Hanbidge M, Driver S, Kroll T, et al. Preparing accessible and understandable clinical research participant information leaflets and consent forms: a set of guidelines from an expert consensus conference. Res Involv Engagem. 2021 Dec;7(1):31.

Appendix 1 – Excluded PIS/ICFs.

Trial Name	Document date	Document Version	Sponsor	Study Design	Study Phase	Exclusion Reason
ABRA	06/03/2023	5.0	University of Oxford (AstraZeneca Unrestricted Grant)	Randomised, Parallel Assignment, Double blind	II	Non-COVID study Document outside screening period
STARR 2	15/06/2017	1.0	University of Oxford	Randomised, Parallel Assignment, Quadruple blind	IV	Non-COVID study Document outside screening period
STOIC	13/05/2020	1.0	University of Oxford	Randomised, Parallel Assignment, Open label	II	Outpatient clinical setting

Appendix 2- Trial Summary information

Trial Name	Document	Document	Sponsor	Study Design	Study	Recruitment	Intervention	Additional

	date	Version			Phase	target	(Route of delivery)	notes
ReCOVERY	17/03/2020	1.4	Academic (University of Oxford, Oxford)	Randomised, Factorial assignment, Open label	III (Platform)	50000	Lopinavir-Ritonavir (oral) Interferon (inhaled) Dexamethasone (Intavenous/Oral)	Translations available.
REMAP-CAP	09/04/2020	1.3	Academic (University Medical Centre, Utrecht)	Randomised, Adaptive Bayesian Platform Trial evaluating multiple interventions in multiple domains. Open Label.	III (Platform)	10000	Multiple (Intravenous, Oral)	6 potential interventions, run concurrently based on clinical factors.
TACTIC-E	03/06/2020	1.1	Academic (Cambridge University Hospitals NHS Trust, Cambridge)	Randomised, Parallel assignment, Open label	II/III (Platform)	1407	EDP1815 (oral) Dapagliflozen (oral) Ambrisentan (oral)	Part A / Part B format
TACTIC-R	04/05/2020	1.2	Academic (Cambridge University Hospitals NHS Trust, Cambridge)	Randomised, Parallel assignment, Open label	III (Platform)	1167	Ravulizumab (Intravenous) Baricitinib (oral)	Part A / Part B format
GS-US-540-5773	27/03/2020	3	Gilead	Randomised, Parallel Assignment, Open label	III	400	Remdesevir (Intravenous)	
RUXCOVID	23/04/2020	0	Novartis	Randomized,	III	402	Ruxolitinib (Oral)	Offered

				Double-blind, Placebo-controlled				summary sheet.
ACCORD-2	30/04/2020	1.2	Academic (University of Southampton)	Adaptive Randomisation, Platform study, Open label.	II	1800	Bemcentinib (Oral)	Offered summary sheet.
COVASE	24/04/2020	2	Academic (University College London Hospitals NHS)	Randomised, parallel assignment, open-label.	II	50	Dornase Alpha (nebulised)	Offered summary sheet.
ILEAD-7	06/05/2020	3	Revimmune	Randomised, Placebo, Quadruple-Blind.	II	48	Interleukin-7 (Intramuscular)	UK cohort of international study.
OSCAR GSK	01/05/2020	1	GlaxoSmithKline	Randomised, Placebo, Double-Blind.	II	800	Otilimab (Intravenous)	Offered summary sheet.
SPRINTER	26/10/2020	1	Synairgen Research Ltd.	Randomised, Double-Blind, Parallel Assignment.	III	610	SNG001 (Inhaled)	
SYNAIRGEN SG016	13/03/2020	2	Synairgen Research Ltd.	Randomised, Quadruple-blind Parallel Assignment.	II	220	SNG001 (Inhaled)	
Theravance 0188	18/05/2020	3	Theravance Biopharma	Randomised, Placebo, Triple-Blind.	II	159	TD-0903 (inhaled)	

Appendix 3 – Subsection Analysis

Trial	Privacy and Information Governance section		Benefits section		Risks section	
	Words	Reading time	Words	Reading time	Words	Reading time

		(mins, 240 wpm)		(mins, 240 wpm)		(mins, 240 wpm)
Phase III Academic (Platform trials)						
ReCOVERY	72	0.3	42	0.2	96	0.4
REMAP-CAP	661	2.8	133	0.6	328	1.4
TACTIC-E	517	2.2	41	0.2	573	2.4
TACTIC-R	519	2.2	41	0.2	255	1.1
Phase III Commercial						
GS-US-540-5773	988	4.1	85	0.4	495	2.1
RUXCOVID	1159	4.8	40	0.2	1189	5.0
SPRINTER	490	2.0	133	0.6	636	2.7
Phase II Trials						
ACCORD-2	968	4.0	0	0	949	4.0
COVASE	355	1.5	41	0.2	297	1.2
ILEAD-7	331	1.4	101	0.4	287	1.2
OSCAR GSK	531	2.2	125	0.5	801	3.3
SYNAIRGEN SG016	709	3.0	48	0.2	668	2.8
Theravance 0188	469	2.0	41	0.2	517	2.2
Overall						

Median	519	2.2	48	0.2	517	2.2

Appendix 4 – Plain English Criteria

Trial Name	Average Sentence Length (words)	Text in passive tense (%)	Avoids Capitals	Bullet Points	Avoids Underlining
ReCOVERY	20.5	45%	Yes	No	Yes
REMAP-CAP	18	37%	Yes	No	Yes
TACTIC-E	20.5	42%	Yes	Yes	No
TACTIC-R	20.1	43%	Yes	Yes	No
GS-US-540-5773	19.4	37%	No	Yes	No

RUXCOVID	18.5	35%	Yes	Yes	No
SPRINTER	20.4	38%	No	Yes	No
ACCORD-2	19.1	41%	Yes	Yes	No
ILEAD-7	20.6	22%	No	Yes	No
OSCAR GSK	16.3	33%	Yes	Yes	No
SYNAIRGEN SG016	18.9	40%	Yes	Yes	No
Theravance 0188	18	40%	No	Yes	No

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Assessment of readability and complexity of written information presented to hospitalised patients for trial consent during the COVID-19 pandemic in the United Kingdom, a retrospective document analysis.

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Readability and complexity of written information presented to hospitalised patients for trial consent during the COVID-19 pandemic in the United Kingdom: a retrospective document analysis.

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Abstract

- **Objectives:** Patient Information Sheets (PIS) and Informed Consent Forms (ICF) are essential tools to communicate and document informed consent for clinical trial participation. These documents need to be easily understandable, especially when used to take informed consent from acutely unwell patients. Health literacy guidance recommends written information

should be at a level between reading age 9 to 11. We aimed to assess the readability and complexity of PIS/ICFs used for clinical trials of acute therapies during the COVID-19 pandemic.

- **Design:** Retrospective document analysis.
- **Setting:** PIS/ICFs used in trials involving pharmaceutical interventions recruiting hospitalised patients with COVID-19 during the first year of the pandemic were sourced from hospitals across the UK
- **Primary and secondary outcome measures:** PIF/ICFs were assessed for length, approximate reading time and subsection content. Readability and language complexity were assessed using Flesch-Kincaid Grade Level (FKGL) (range 1-18; higher is more complex), Gunning-Fog (GFOG) (range 1-20; higher is more complex) and Flesch Reading Ease Score (FRES) (range 0-100; below 60 is 'difficult' for comprehension).
- **Results:** Thirteen documents were analysed with a median length of 5139 words (range 1559–7026), equating to a median reading time of 21.4 minutes (range 6.5–29.3 minutes) at 240 words per minute. Median FKGL was 9.8 (9.1–10.8), GFOG 11.7 (10.4-13) and FRES was 54.6 (47.0–58.3). All documents were classified as 'difficult' for comprehension and had a reading age of 14 years old or higher.
- **Conclusions:** All PIS/ICFs analysed contained literary complexity beyond both recommendations and the reading level of many in the UK population. Researchers should seek to improve communications to improve trial volunteer comprehension and recruitment.

Strengths and limitations of this study

- This study analyses PIS/ICF content and readability using commonly used and objective methods.
- It uses transparent and identifiable results at individual trial level
- As a retrospective synthetic analysis, it cannot assess actual patient understanding and opinions at the time of illness/recruitment.
- PIS/ICF components such as diagrams and other visual elements were not analysed

Introduction

The COVID-19 pandemic of 2020 saw research trials set up rapidly to be delivered in acute care settings, often by staff with limited prior trials experience and involving acutely unwell patients. This created new challenges for trials staff and patients[1]. The suitability of the consent processes has been identified as one of the main concerns around the research response to the pandemic[2]. Patient Information Sheet (PIS) and Informed Consent Forms (ICF) were adapted from conventional trial templates, following standard UK Medicines and Healthcare Products Regulatory Agency (MHRA) recommendations[3]. Trials staff identified that PIS/ICFs were not suited to the circumstances in which consent and trial discussions actually took place, typically involving staff in masks and personal protective equipment (PPE) and patients who were very unwell, afraid, and isolated from family [2].

Informed consent is both a legal and ethical requirement for healthcare research[4] and is a cornerstone of Good Clinical Practice [5]. For trials involving investigational medicinal products (IMPs) there is a legal requirement for written consent to be obtained, unless not physically possible and specifically exempted[6]. UK and international guidelines state that the written information provided to participants should support conversations around consent, rather than being the sole source of information[3]. This is usually provided in the form of a PIS/ICF, often the only written record provided to patients involved in clinical trials.

Increasing length and language complexity of consent forms may correlate with decreasing participant comprehension [7,8]. Despite this, PIS/ICFs have become longer and more complex over time[9], reflecting the requirements of sponsors, ethical review boards and/or recommendations from patients. The implementation of European Union (EU) General Data Protection Regulations (GDPR) has further extended documents[10]. Additional considerations regarding consent for samples stored for future use and for genetic testing has added further complexity[11]. A consequence of this is that after recruitment clinical trials participants often do not retain an understanding of key components of studies[12,13].

In response to the issues raised by trials staff delivering studies in acute settings during the pandemic, we were interested to review the information provided to trials participants to help understand the problem and identify whether there are better ways to deliver this. The objectives of this study were to describe the written information presented to participants in acute COVID-19 trials in terms of length, content, and readability.

Methods

Patient Information Sheet and Informed Consent Forms for acute inpatient COVID trials were requested from trials teams across NIHR Respiratory Translational Research Collaboration (TRC) UK sites via email. PIS/ICFs were reviewed by the lead author to ensure only trials involving investigational medical products administered to hospital inpatients were included. PIS/ICFs involving personal legal representative, professional legal representative, or deferred consent, such as for patients lacking capacity, were excluded. Documents were excluded if published after March 2021. Trials teams were further contacted via email to clarify availability of translated documents, acceptability of telephone translation, and availability of supplementary information sources during the screening period.

All PIS/ICFs were received as Microsoft Word .doc or .docx files. Total page count was recorded, then documents were prepared for further analysis in line with guidelines for conducting readability analyses by the Centres for Medicare and Medicaid Services [14](full details in supplement).

Document length was analysed via total word count. Approximate time-to-read was calculated based on an average reading speed of 240 words per minute (wpm), as well as upper and lower ranges (175-300 wpm). Reading speed estimates are based on analysis by *Brysbaert* for adults reading silently[15]. PIS subsections were reviewed and recorded. Subsections covering privacy and information governance, benefits of participation, and risks of participation were individually analysed by total word count.

Language complexity was analysed using the Flesch-Kincaid Grade Level (FKGL) assessment. This metric assesses both word and sentence length and is expressed as a score (range 1-18; higher is more complex), equivalent to US school grade level reading age (Table 1)[16]. Readability was assessed using the Flesch Reading Ease Score (FRES) (range 0-100; below 60 is 'difficult') and the Gunning-Fog Index (GFOG) (range 1-20; higher is more complex). Both metrics assess readability by analysing word complexity and sentence length. There are over 200 readability metrics, with no definitive best metric for either general or health literature[17]. These three metrics were selected as they are long established and commonly used allowing comparison with a large number of previous studies[18], including recent relavent research such as *Emmanuel & Boyle* (22) *and O'Sullivan et al*[10].

Documents were also assessed against the objectively assessable Plain English recommendations for written medical information[19]. These consisted of: recommended sentence length 15-20 words; no more than 10% of writing in passive tense; avoiding writing headings in all capitals; avoids underlining; appropriate use of bullet points.

Analysis software

Total pages, total word count, subsection word count, sentence length and passive tense percentage were calculated using Microsoft Word (Mac version 16.69.1, performed in June 2023). FKGL, FRES and GFOG were calculated using Readable (Added Bytes Ltd, Horsham, UK, accessed June 2023) [20] by uploading each prepared document following preparation.

Statistical analyses are descriptive. Data were tested for normality using the Shapiro-Wilk test in GraphPad Prism version 9.0 for Macintosh (GraphPad Software, www.graphpad.com) and presented as median (interquartile range)

Ethical Approval

This study did not require REC approval in line with HRA guidelines (https://www.hra-decisiontools.org.uk/research/). All PIS/ICFs received for analysis were for trials that had received a positive ethical review.

Public and patient involvement

Patients and the public were not involved in the design of this study.

Age	US Grade Level	English School equivalent	Flesh Kincaid Grade Level	Gunning Fog Index Score	Flesh Reading Ease Score
6-7	1	Year 2	1	1	
7-8	2	Year 3	2	2	
8-9	3	Year 4	3	3	
9-10	4	Year 5	4	4	
10-11	5	Year 6	5	5	90-100
11-12	6	Year 7	6	6	80-90
12-13	7	Year 8	7	7	70-80
13-14	8	Year 9	8	8	60-70
14-15	9	GCSE	9	9	
15-16	10		10	10	50-60
16-17	11	A Levels	11	11	

17-18	12		12	12	30-50
	University (Year 1-3)		13-15	13-15	
	University (Year 4)		16	16	
	Post-graduate		17-18	17-20	0-30
	Post graduate plus			>20	

Table 1: Readability scores with equivalent age, English & US school grades. [18] [21]

Results

We have included information sheets from thirteen clinical trials meeting inclusion criteria. Three supplied PIS/ICFs were excluded (supplement). Of the analysed documents six were phase 2 trials, three were commercial, single agent phase 3 studies and four were phase 3 platform studies (supplement). Four studies offered trial summary sheets for patients to read prior to the longer PIS/ICF. Translated PIS/ICFs were available for the RECOVERY trial PIS in 2020, though REMAP-CAP also introduced translated documents for UK use in 2021.

1. Document length

Median (range) word count for the analysed combined PIS and ICF documents was 5139 words (range 1559 – 7026) (Table 2). For a participant with a mean average reading speed (240 wpm) this length equates to a reading time of 21.4 minutes (range 6.5– 29.3 minutes). Participants reading at the lower bound reading speed (175wpm) would take on average 29.4 minutes (range 8.9 – 40.1 minutes). Unlike the other trials included in this analysis, the RECOVERY trial PIS/ICF contained only generic text on IMP risks and was therefore notably shorter in length.

2. Subsection Content

Subsection analysis revealed marked variation in length (supplement). Information relating to privacy and information governance ranged from 72 to 1159 words in total (reading time 0.3 – 4.0 minutes), with a median of 519 words. The section on risks of participation ranged from 92 to 1189 words (reading time 0.4 - 5.0 mins), with a median of 519. All trials featured a short section on patient benefits of the research (median 48, range 0 -133 words), except for the ACCORD-2 study.

3. Language complexity

All information sheets featured notable language complexity, median (range) 9.8 (9.1 – 10.8), with no document scoring lower than a Flesch-Kincaid Grade Level of 9, equivalent to that of a 14-15 year old (Table 1).

4. Readability

None of the included PIS scored above 60 on FRES, with a median (range) score of 54.6 (47.0 – 58.3). Scores below 60 are considered 'difficult' for comprehension, with scores 50-60 equating to 15-17 year old reading level.. Assessing readability using the alternative measure the Gunning-Fog index (GFOG), the documents had a median (range) score of 11.7 (10.4 – 13.0). A score of 11 is equivalent to reading age 16-17 (Table 1).

5. Use of plain English

Three out of thirteen trial PIS had an average sentence length greater than 20. All trial PIS exceeded the recommended 10% writing in passive tense, with a median (range) of 40% (22% - 41%). Three out of 13 trials presented headings in capitals, while two out of 13 trials did not use bullet points. 10 trials used underlining. No trial met all five assessed Plain English recommendations (Supplement).

Trial	Total Words	Reading Time (minutes)			Flesch-Kincaid Grade Level[1]	Gunning-Fog score[2]	Flesch Reading Ease Score[3]	Average Sentence Length (words)
		175 wpm (lower bound)	240 wpm (mean)	300 wpm (upper bound)				
Phase III Platform trials								
RECOVERY	1559	8.9	6.5	5.2	9.9	12.2	55.2	20.5
REMAP-CAP	3688	21.1	15.4	12.3	10.5	12.1	48.2	18
TACTIC-E	5685	32.5	23.7	19.0	10.6	12.4	49.1	20.5
TACTIC-R	4994	28.5	20.8	16.6	10.8	12.7	48.9	20.1
Phase III Single Agent Commercial								
GS-US-540-5773	5139	29.4	21.4	17.1	9.1	10.6	57.8	19.4
RUXCOVID	6855	39.2	28.6	22.9	9.2	10.4	55.0	18.5
SPRINTER	5467	31.2	22.8	19.1	9.8	11.8	54.4	20.4
Phase II								
ACCORD-2	7026	40.1	29.3	23.4	10.0	11.9	54.6	19.1
COVASE	3544	20.3	14.8	11.8	9.7	11.3	54.8	18.9
ILEAD-7	4626	26.4	19.3	15.4	11.2	13.0	47.0	20.6
OSCAR GSK	6046	34.5	25.2	20.2	9.3	11.6	56.5	16.3
SYNAIRGEN SG016	6455	36.9	26.9	21.7	9.0	11.2	58.3	18.9
Theravance 0188	4468	25.5	18.6	14.9	9.7	11.6	54.2	18
Overall								
Median	5139	29.4	21.4	17.1	9.8	11.8	54.6	19.1

Table 2: Summary of document length and complexity for clinical trial patient information sheets (PIS) and investigator consent forms (ICF) for clinical trials conducted during acute COVID-19 infection. [1]Range 0-18, higher score is more complex, recommended ≤6. [2]Range 0-20, higher score is less readable, recommended ≤6. [3]Range 0-100, 100 is best readability, recommended ≥60.

Discussion

In this study we have analysed the information provided to hospitalised patients undergoing recruitment to trials of new therapies for COVID-19. The pandemic was an unprecedented international health emergency, and there was urgent need for potential therapies to be trialled in these settings. Trials staff identified that consent processes were often ill suited to the acute settings in which they were delivered(1). Our results would appear to support these subjective observations. Median length was 5303 words, equivalent to a reading time of 21.4 minutes, though this is likely an underestimate of the true time patients would require. Reading time estimates are derived from studies in healthy volunteers and do not take into account pauses or re-reading of sections[15]. There is no data available quantifying the impact of acute illness states on reading speed or accuracy. In this state median reading time may be nearer the lower reading speed estimate of 29.6 minutes.

Long and complex PIS/ICFs are not unique to this clinical scenario with similar findings for paediatric trials[22], surgical trials[23] and trials conducted in emergency departments[24]. *O'Sullivan* analysed 176 PIS/ICFs used in the UK and Ireland up to 2019, demonstrating readability metrics similar to those found in this analysis[10]. Similar issues were also identified by a US study looking at consent and patient information for COVID vaccine studies delivered in non-acute settings [25]. This highlights that these COVID studies had very little adaptation for the acute scenario from standard practice. While the longest and most complex documents were phase II trials, this was not universal with three phase II trials being below the overall median for both length and four for language complexity. HRA/MHRA guidance requires PIS/ICFs involving Investigational Medicinal Products (IMPs) to contain specific information[26], potentially limiting the minimum practical document length. Given the wide range of document word lengths 1559 – 7026) it is likely that it would be legally possible to substantially reduce most documents analysed.

Literacy skills in the United Kingdom vary widely. The UK Government Skills for Life survey in 2011 found that 15% of people in England aged 16-65 had reading ability below adult literacy 'level 1', broadly equivalent to a reading age of 12-14 years old. Accordingly 1 in 6 individuals would not attain a grade D-G at GCSE level English and would likely struggle to read a train timetable or a pay slip[27]. In contrast, the information provided in the trial patient information sheets had a median complexity equivalent to age 14-15 years and median readability was equivalent to age 16-17 years.

Written PIS are only one part of the consent process, and informed consent also involves a trained health professional delivering the information and contextualising this for participants[26]. In normal practice this is relatively straightforward, involving discussion with the patient, sometimes with family members too, to ensure that they understand the study, including risks and benefits. In the specific context of the COVID-19 pandemic however staff were required to wear PPE, including masks and face

protectors. While necessary to protect staff, studies have shown that wearing PPE, particularly masks, have a negative effect on speech discrimination and comprehension[28,29]. For this reason, providing clear and accessible written information for COVID-19 trials was even more important.

During the early months of the pandemic there were no approved therapies for COVID-19, beyond best supportive care. Patients in the UK did not have access to the wide range of therapies that were being proposed and offered elsewhere without trial evidence[30]. The only way of accessing such treatments was in the context of a trial, and patients may have felt particularly incentivised to take part in trials because of this. This may have mitigated against impact of information being only partially understood. It does not detract however from the need to reflect on this aspect of clinical trials in order to understand how to improve the information provided in acute settings.

Four of the included studies also provided a trial summary sheet for patients, so that they could review the most important points of the trial without reference to the much longer full PIS. No other forms of information were available, and none of the studies made use of video explainers during the first year of the pandemic. The RECOVERY study did offer information for patients online[31], while the TACTIC trials published videos online in late 2021[32]. Future trials may consider looking at how to use such resources to better inform patients, and clinical trial templates for acute settings might benefit from being more concise and focussed. To support rapid progression of medical knowledge during pandemics or other national emergencies, there might be a case for more streamlined consent processes. For example, a two-stage consent might present the most important points only in the acute presentation, followed by a review of consent and confirmation of participation during convalescence.

This study has only looked at the information provided to patients in written form, and a limitation is that we are unable to assess now how this was viewed and retained by patients at the time. We have also only looked at information provided in English, and the analyses of reading time and complexity all assume that English is the reader's first language. We are unable to assess how many patients would have had added difficulty because this was not the case. No data are available on how many, if any, patients were excluded by inability to fully comprehend written or verbally provided information. Only the two major platform studies had translated documents available. The RECOVERY trial allowed telephone translations if a patient's native translation was not available in written form, though no others did. Following correspondence with trial sites we are aware of sites being unwilling to enrol patients in RECOVERY without endorsed written documents. *Murali* showed Asian, Black and Mixed ethnic groups were underrepresented in UK Covid-19 trials[33]. While the causes of this are multifaceted, it is likely that language issues were a contributory factor. We have deliberately not compared these consent forms to those used in other acute settings, since the primary focus was to

address how consent was delivered during COVID-19 to reflect how we can better manage future pandemics. These finding are however likely generalisable to other acute settings. Synthetic reliability metrics have inherent limitations such as not assessing layout or non-text components of documents such as diagrams. Furthermore documents rewritten with improved readability scores do not always improve participant comprehension[34]. Nonetheless their use has been endorsed to guide improvements in readability of PIS/ICFs following consensus meetings[35].

In summary, we have shown that clinical trial participant information sheets are lengthy, take significant time to read under optimal conditions, and regularly exceed recommendations on complexity and language. In acute settings it is especially important to make the communication of trials information clear and understandable. Patient information and consent was identified as being an area for improvement by clinical trials staff. In collaboration with patients and public contributors, proportionate information sheets for acute settings need to be developed with alternative consenting models considered which include multi-step process where complex information is only delivered when patients are well enough to consider it.

Data Availability

Data are available upon reasonable request

All documents and analysis data are available on request from Dr Ewan Gourlay (Orcid: https://orcid.org/0000-0002-0905-8247)

Author Contributions

Conceptualisation by AH. Data collection and initial analysis by EG. Manuscript initially drafted by EG and AH. Significant critical review and further development of manuscript by all authors. All authors approve final copy. AH is the guarantor of this work.

Competing Interests

MB reports unrestricted research grants from AstraZeneca and Roche, and has received honoraria to her institution for speaker's fees from AstraZeneca, Chiesi, Cipla and GlaxoSmithKline. She is a scientific adviser to Albus Health and ProAxsi. CEB reports fees to his institution from AZ, GSK, Novartis, Chiesi, BI, Genentech, Roche, Sanofi, Regeneron, Mologics, 4DPharma, Synairgen, Merck. JCD reports reports grants from CF Trust, CF Foundation, CF Ireland, EPSRC and personal fees Vertex Pharmaceuticals, Boehringer-Ingelheim, Eloxx, Algipharma, Abbvie, Arcturus, Enterprise Therapeutics. RAE reports grants from NIHR/UKRI/Wolfson Foundation; consulting fees from AstraZeneca; lecture honoraria from Boehringer; travel support from Chiesi. LPH reports grants from MRC. SM reports grants from BLF, MRC, June Hancock Mesothelioma Research, Alpha-1 Foundation, and Myrovlytis Trust. NM reports unrestricted research grants from and sits on paid advisory boards

for Rocket Medical Plc and BD. JCP reports grants from UKRI, LifeArc and MRC. ES reports reports grant funding from NIHR, MRC, HDR-UK, Innovate UK, British Lung Foundation and Alpha 1 Foundation. SS reports speaker fees from GSK, AstraZeneca, Chiesi, Boehringer Ingelheim, and Novartis; participates on advisory boards for GSK, AstraZeneca, Chiesi, Boehringer Ingelheim, Novartis, Knopp Biotech, Munipharma, ERT Medical, and Owlstone Medical; is a member of the European Respiratory Society Science Council and the UK Medical Research Council; and is a cofounder of Eupnoos Ltd. TW reports grants from UKRI, Synairgen, AZ, UCB, Bergenbio and personal fees from Synairgen and Valneva. ARH reports grants from JP Moulton Charity, CF Trust, CF Foundationinfor, MRC and UKRI and personal fees from Vertex Pharmaceuticals and Mylan Pharmaceuticals

References

1 Mitchell EJ, Ahmed K, Breeman S, *et al.* It is unprecedented: trial management during the COVID-19 pandemic and beyond. *Trials*. 2020;21:784. doi: 10.1186/s13063-020-04711-6

2 Horsley AR, Pearmain L, Knight S, *et al.* Large scale clinical trials: lessons from the COVID-19 pandemic. *BMJ Open Respir Res*. 2022;9:e001226. doi: 10.1136/bmjresp-2022-001226

3 General Principles - Consent and Participant information sheet preparation guidance. Health Research Authority. https://www.hra-decisiontools.org.uk/consent/principles-general.html (accessed 13 February 2023)

4 World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *Jama*. 2013;310:2191–4.

5 ICH guideline for good clinical practice E6(R2). International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. 2016. Available: https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice-scientific-guideline

6 Informed consent in clinical trials. UK Health Research Authority. 2008. Available: www.hra.nhs.uk/media/documents/informed-consent-in-ctimps.pdf

7 Grundner TM. On the Readability of Surgical Consent Forms. *N Engl J Med*. 1980;302:900–2. doi: 10.1056/NEJM198004173021606

8 Epstein LC. Obtaining Informed Consent: Form or Substance. *Arch Intern Med*. 1969;123:682. doi: 10.1001/archinte.1969.00300160072011

9 Albala I, Doyle M, Appelbaum PS. The evolution of consent forms for research: a quarter century of changes. *IRB Ethics Hum Res*. 2010;32:7–11.

10 O'Sullivan L, Sukumar P, Crowley R, *et al.* Readability and understandability of clinical research patient information leaflets and consent forms in Ireland and the UK: a retrospective quantitative analysis. *BMJ Open*. 2020;10:e037994. doi: 10.1136/bmjopen-2020-037994

11 Code of Practice and Standards - Code E : Research. Human Tissue Authority. 2017. Available: https://content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf (accessed 13 February 2023)

12 Foe G, Larson EL. Reading Level and Comprehension of Research Consent Forms: An Integrative Review. *J Empir Res Hum Res Ethics*. 2016;11:31–46. doi: 10.1177/1556264616637483

13 Kelly CM, Feighery R, McCaffrey J, *et al.* Do oncology patients understand clinical trials? A nationwide study by Cancer Trials Ireland. *Ann Oncol*. 2017;28:v643–4. doi: 10.1093/annonc/mdx440.068

14 Toolkit for Making Written Material Clear and Effective - Part 7 : Using readability formulas: A cautionary note. U.S. Department of Health and Human Services Centers for Medicare & Medicaid Services. 2010. Avaialble: https://montefioreeinstein.org/documents/ToolkitPart07.pdf (accessed 13 February 2023)

15 Brysbaert M. How many words do we read per minute? A review and meta-analysis of reading rate. *J Mem Lang*. 2019;109:104047. doi: 10.1016/j.jml.2019.104047

16 Jindal P, MacDermid J. Assessing reading levels of health information: uses and limitations of flesch formula. *Educ Health*. 2017;30:84. doi: 10.4103/1357-6283.210517

17 DuBay WH. *The Principles of Readability*. Impact Information 2004.

18 Kincaid JP, Fishburne Jr, Robert P. R, *et al.* Derivation of New Readability Formulas (Automated Readability Index, Fog Count and Flesch Reading Ease Formula) for Navy Enlisted Personnel: Fort Belvoir, VA: Defense Technical Information Center 1975.

19 Medical information. Plain English Campain. https://www.plainenglish.co.uk/medical-information.html (accessed 13 February 2023)

20 Test your readability. Readable. https://readable.com/ (accessed 13 February 2023)

21 Flesch R. *The Art of Readable Writing (Reissue)*. Wiley-Hungry Minds 1949.

22 Nash E, Bickerstaff M, Chetwynd AJ, *et al.* The readability of parent information leaflets in paediatric studies. *Pediatr Res*. 2023;94:1166–71. doi: 10.1038/s41390-023-02608-z

23 Karimi AH, Guyler MR, Hecht CJ, *et al.* Assessing the Readability of Clinical Trial Consent Forms for Surgical Specialties. *J Surg Res*. 2024;296:711–9. doi: 10.1016/j.jss.2024.01.045

24 Mader TJ, Playe SJ. Emergency Medicine Research Consent Form Readability Assessment. *Ann Emerg Med*. 1997;29:534–9. doi: 10.1016/S0196-0644(97)70229-4

25 Emanuel EJ, Boyle CW. Assessment of Length and Readability of Informed Consent Documents for COVID-19 Vaccine Trials. *JAMA Netw Open*. 2021;4:e2110843. doi: 10.1001/jamanetworkopen.2021.10843

26 Applying a proportionate approach to the process of seeking consent. Health Research Authority. 2018.

27 2011 Skills for Life Survey: A Survey of Literacy, Numeracy and ICT Levels in England. 2011.

28 Round M, Isherwood P. Speech intelligibility in respiratory protective equipment - Implications for verbal communication in critical care. *Trends Anaesth Crit Care*. 2021;36:23–9. doi: 10.1016/j.tacc.2020.08.006

29 Hampton T, Crunkhorn R, Lowe N, *et al.* The negative impact of wearing personal protective equipment on communication during coronavirus disease 2019. *J Laryngol Otol*. 2020;134:577–81. doi: 10.1017/S0022215120001437

30 Coffey B. COVID-19: A Research Timeline. Royal Society of Medicine. 2022. Available: https://cms.rsm.ac.uk/media/5477551/covid-19_two-years-on_a-research-timeline-dec2022.pdf (accessed 8th Jan 2025)

31 For patients in the UK : RECOVERY Trial. University of Oxford. https://www.recoverytrial.net/uk/study-faq. (accessed 8th Jan 2025)

32 COVID-19 Clinical Trials : TACTIC-E. Youtube 2021. Available: https://www.youtube.com/watch?v=Mz8VtNuDF-I. (accessed 8th Febuary 2024)

33 Murali M, Gumber L, Jethwa H, *et al.* Ethnic minority representation in UK COVID-19 trials: systematic review and meta-analysis. *BMC Med*. 2023;21:111. doi: 10.1186/s12916-023-02809-7

34 Grady C, Touloumi G, Walker AS, *et al.* A randomized trial comparing concise and standard consent forms in the START trial. *PLOS ONE*. 2017;12:e0172607. doi: 10.1371/journal.pone.0172607

35 Coleman E, O'Sullivan L, Crowley R, *et al.* Preparing accessible and understandable clinical research participant information leaflets and consent forms: a set of guidelines from an expert consensus conference. *Res Involv Engagem*. 2021;7:31. doi: 10.1186/s40900-021-00265-2

Supplement

Text Preparation

Documents were prepared for analysis following Centres for Medicare and Medicaid Services guidelines (2010) prior to using readability calculators(1). Incomplete sentences were removed, with full stops added to the end of any headings and incomplete sentence bullet points. URLs were replaced with the word “website’. Midsentence full stops e.g. “U.K.” were removed. In addition, text based tables using characters, most commonly ‘x’ to indicate trial interventions at different time points were removed.

Excluded PIS/ICFs.

Trial Name	Document date	Document Version	Sponsor	Study Design	Study Phase	Exclusion Reason
ABRA	06/03/2023	5.0	University of Oxford (AstraZeneca Unrestricted Grant)	Randomised, Parallel Assignment, Double blind	II	Non-COVID study Document ou[illegible] screening pe[illegible]
STARR 2	15/06/2017	1.0	University of Oxford	Randomised, Parallel Assignment, Quadruple blind	IV	Non-COVID study Document ou[illegible] screening pe[illegible]
STOIC	13/05/2020	1.0	University of Oxford	Randomised, Parallel Assignment, Open label	II	Outpatient [illegible]al setting

Trial Summary information

Trial Name	Document date	Document Version	Sponsor	Study Design	Study Phase	Recruitment target	Intervention (Route of delivery)	Additional notes

RECOVERY	17/03/2020	1.4	Academic (University of Oxford, Oxford)	Randomised, Factorial assignment, Open label	III (Platform)	50000	Lopinavir-Ritonavir (oral) Interferon (inhaled) Dexamethasone (Intavenous/Oral)	Translations available.
REMAP-CAP	09/04/2020	1.3	Academic (University Medical Centre, Utrecht)	Randomised, Adaptive Bayesian Platform Trial evaluating multiple interventions in multiple domains. Open Label.	III (Platform)	10000	Multiple (Intravenous, Oral)	6 potential interventions, run concurrently based on clinical factors.
TACTIC-E	03/06/2020	1.1	Academic (Cambridge University Hospitals NHS Trust, Cambridge)	Randomised, Parallel assignment, Open label	II/III (Platform)	1407	EDP1815 (oral) Dapagliflozen (oral) Ambrisentan (oral)	Part A / Part B format
TACTIC-R	04/05/2020	1.2	Academic (Cambridge University Hospitals NHS Trust, Cambridge)	Randomised, Parallel assignment, Open label	III (Platform)	1167	Ravulizumab (Intravenous) Baricitinib (oral)	Part A / Part B format
GS-US-540-5773	27/03/2020	3	Gilead	Randomised, Parallel Assignment, Open label	III	400	Remdesevir (Intravenous)	
RUXCOVID	23/04/2020	0	Novartis	Randomized, Double-blind,	III	402	Ruxolitinib (Oral)	Offered summary sheet.

				Placebo-controlled				
ACCORD-2	30/04/2020	1.2	Academic (University of Southampton)	Adaptive Randomisation, Platform study, Open label.	II	1800	Bemcentinib (Oral)	Offered summary sheet.
COVASE	24/04/2020	2	Academic (University College London Hospitals NHS)	Randomised, parallel assignment, open-label.	II	50	Dornase Alpha (nebulised)	Offered summary sheet.
ILEAD-7	06/05/2020	3	Revimmune	Randomised, Placebo, Quadruple-Blind.	II	48	Interleukin-7 (Intramuscular)	UK cohort of international study.
OSCAR GSK	01/05/2020	1	GlaxoSmithKline	Randomised, Placebo, Double-Blind.	II	800	Otilimab (Intravenous)	Offered summary sheet.
SPRINTER	26/10/2020	1	Synairgen Research Ltd.	Randomised, Double-Blind, Parallel Assignment.	III	610	SNG001 (Inhaled)	
SYNAIRGEN SG016	13/03/2020	2	Synairgen Research Ltd.	Randomised, Quadruple-blind Parallel Assignment.	II	220	SNG001 (Inhaled)	
Theravance 0188	18/05/2020	3	Theravance Biopharma	Randomised, Placebo, Triple-Blind.	II	159	TD-0903 (inhaled)	

Page totals & Subsection Analysis

Trial	Total Page Count		Privacy and Information Governance section		Benefits section		Risks section	
	PIS	ICF	Reading time (mins,	Words	Reading time	Words	Reading time	Words

			240 wpm)		(mins, 240 wpm)		(mins, 240 wpm)	
Phase III Platform trials								
RECOVERY	2	2	72	0.3	42	0.2	96	4
REMAP-CAP	8	2	661	2.8	133	0.6	328	4
TACTIC-E	13	3	517	2.2	41	0.2	573	4
TACTIC-R	9	3	519	2.2	41	0.2	255	1
Phase III Commercial								
GS-US-540-5773	13	3	988	4.1	85	0.4	495	1
RUXCOVID	14	4	1159	4.8	40	0.2	1189	0
SPRINTER	12	2	490	2.0	133	0.6	636	7
Phase II Trials								
ACCORD-2	14	4	968	4.0	0	0	949	0
COVASE	5	2	355	1.5	41	0.2	297	2
ILEAD-7	10	2	331	1.4	101	0.4	287	2
OSCAR GSK	20	5	531	2.2	125	0.5	801	3
SYNAIRGEN SG016	15	3	709	3.0	48	0.2	668	8
Theravance 0188	10	2	469	2.0	41	0.2	517	2
Overall								
Median	12.5	3	519	2.2	48	0.2	517	2

Plain English Criteria

Trial Name	Average Sentence Length (words)	Text in passive tense (%)	Avoids Capitals	Bullet Points	Avoids Underlining
RECOVERY	20.5	45%	Yes	No	Yes
REMAP-CAP	18	37%	Yes	No	Yes
TACTIC-E	20.5	42%	Yes	Yes	No
TACTIC-R	20.1	43%	Yes	Yes	No
GS-US-540-5773	19.4	37%	No	Yes	No
RUXCOVID	18.5	35%	Yes	Yes	No
SPRINTER	20.4	38%	No	Yes	No
ACCORD-2	19.1	41%	Yes	Yes	No

ILEAD-7	20.6	22%	No	Yes	No
OSCAR GSK	16.3	33%	Yes	Yes	No
SYNAIRGEN SG016	18.9	40%	Yes	Yes	No
Theravance 0188	18	40%	No	Yes	No

1. Toolkit for Making Written Material Clear and Effective - Part 7 : Using readability formulas: A cautionary note [Internet]. U.S. Department of Health and Human Services Centers for Medicare & Medicaid Services; 2010. Available from: https://montefioreeinstein.org/documents/ToolkitPart07.pdf